

### **REMARKS**

Claims 4 to 11 have been rejected under 35 USC § 103 as allegedly being unpatentable over American Journal of Veterinary Research, Vol. 35, pp. 267-73, 1974 by Wooley et al (Wooley) taken with US 5,298,614 to Yano et al (Yano 1) in further view of EP 0685457A1 to Yano et al (Yano 2).

Applicants respectfully disagree with the Examiner and reconsideration of this rejection is respectfully requested.

Initially, applicants would point out that Canine hepatitis is quite different from the human variety. However, that little matters for the present invention. The effectiveness of the present invention for human hepatitis is shown indirectly by the amount of interferon induced by poly I-poly C. These documents showing that interferon is induced even in canine has some relevance to the present invention.

Needless to say, a person skilled in the art would have realized that poly I-poly C is effective for human hepatitis because it is well known that poly I-poly C can induce interferon. However, it is difficult to use poly I-poly C for the practical clinical treatment of hepatitis (e.g. see Background in the present specification). That is because when an effective amount of poly I-poly C is administered to humans, not only is an effective amount of interferon produced, there are also side effects which are induced.

It was almost impossible to reduce side effects while still maintaining the effectiveness of poly I-poly C. Please note Table 1 and Fig. 5 in Machida. Toxicity reduces drastically as the chain length of poly I-poly C is shorter and shorter, but at the same time interferon production also goes down dramatically. Even when poly I-poly C of 4.2S is administered with ten times as much an amount as that of 16S, the plasma level of interferon induced is only 80 units/ml, that is, one-sixtieth of that induced by 16S at 6 hour.

The short-chain-length polynucleotide that Yano illustrates to induce enough interferon is a mismatched poly I-poly C: i.e., poly I-poly (C<sub>20</sub>, S<sup>4</sup>), but poly I-poly C is not illustrated in Yano.

Applicants found that the complex of a short-chain-length poly I-poly C with a cationic liposome can induce an amount of interferon clinically effective for the treatment of hepatitis with lowering side effects (see Test Examples 3 and 4 in the present specification). In addition, since the complex is targeted to the liver, it is advantageous particularly for the treatment of hepatitis (see Test Example 2 in the present specification).

Furthermore, the complex has an unexpected effect. The plasma level at 30 IU/ml of interferon is maintained at 24 hour after the complex is intravenously administered (see Test Example 3 in the present specification). The complex can sustain an enough plasma level of interferon for a long time.

From the view point of the above facts, applicants urge that the present invention is clearly patentable over the prior art relied upon by the Examiner.

Applicants request reconsideration and withdrawal of this § 103 rejection.

It is believed that all of the present claims are in condition for allowance. Early and favorable action by the Examiner is earnestly solicited.

### **CONCLUSION**

Early and favorable action by the Examiner is earnestly solicited. If the Examiner believes that issues may be resolved by a telephone interview, the Examiner is respectfully urged to telephone the undersigned at (212) 801-2146. The undersigned may also be contacted by e-mail at [ecr@gtlaw.com](mailto:ecr@gtlaw.com).

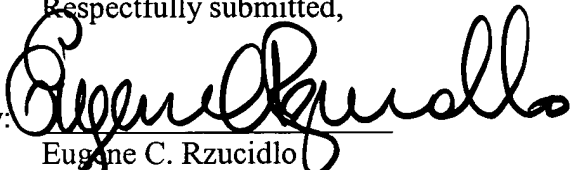
### AUTHORIZATION

If the Examiner believes that issues may be resolved by telephone interview, the Examiner is respectfully urged to telephone the undersigned at (212) 801-2146. The undersigned may also be contacted by e-mail at [ecr@gtlaw.com](mailto:ecr@gtlaw.com).

No additional fee is believed to be necessary. The Commissioner is hereby authorized to charge any additional fees which may be required for this amendment, or credit any overpayment to Deposit Account No. 50-1561.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 50-1561.

Dated: January 8, 2004

Respectfully submitted,  
  
By: Eugene C. Rzucidlo  
Registration No. 31,900  
Customer Number: 32361